## REMARKS

Claims 1-27 are pending. New claim 28 is added. Claims 1, 9, 12,13, 14, 16, 22, 23 are amended.

No amendment introduces new matter.

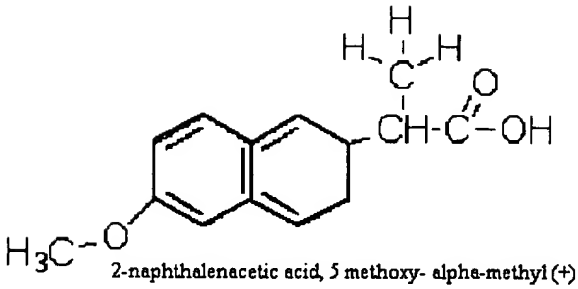
Response to Examiner's Comments

In his Advisory Action, Examiner maintained the rejections and refused to enter the amended claims because he alleges that Desai is prior art. In support, Examiner asserts that "Naproxen and Naproxen sodium as stated in the prior office action are analgesic[sic] that have different chemical properties....Because the two analgesic[sic] have different chemical structures, thus they would have different analgesic characteristics."

Applicants respectfully disagree based on technical knowledge in the art, and because the aforementioned rationale is contrary to longstanding PTO practice.

1. Naproxen and naproxen sodium do not possess different analgesic characteristics. Attachment A, taken from Foye's Medicinal Chemistry states on page 519, col. 2, that "[b]oth naproxen sodium and naproxen circulate in plasma as the *identical dextrorotatory naproxen anion.*" See Desai, col. 1, lines 39-40. Further, it has been shown that the naproxen anion is the chemical species that inhibits prostaglandin synthesis. Attachment B, data sheet from Roche, highlighted text. Thus, *both* forms of naproxen provide the identical active molecular species and thus, are known to have the identical pharmacological effect. In fact, some express caution against taking both naproxen and naproxen sodium because the result may be too high a dose of the same active anion. Attachment C, highlighted text.

As discussed above, Examiner's conclusion that naproxen and naproxen sodium "have different analgesic characteristics" is contradicted by knowledge in the art. Therefore, this rationale for rejecting the claims is improper and should be withdrawn.



2-naphthalenacetic acid, 5 methoxy- alpha-methyl (+)

The chemical basis for both naproxen and naproxen sodium forming the same pharmacologically active anion, is based on the low pKa of the –COOH on the propionic moiety of naproxen. The pKa of naproxen has been reported between 4.2 to 5.0. See e.g., Attachment D, highlighted text. This means that upon contacting neutral or near neutral conditions, the acidic proton dissociates leaving the anion, which is the *identical* anion that is provided by naproxen sodium.

The only difference is that naproxen will dissociate somewhat more slowly than naproxen sodium, thereby resulting in a delayed appearance of the active anion's peak serum levels; usually about 1-2 hours later than naproxen sodium. See Attachment B, 3rd page. However, both compounds provide the same active anion.

In sum, naproxen and naproxen sodium form the same active anion. In Desai's formulation this active anion is formed *from both* of Desai's delayed release layer and immediate release layer. Therefore, it is indisputable that each of the delayed and immediate release layers in Desai's formulation, provide the *identical analgesic* – the naproxen anion.

The amended claims are clearly distinguishable from Desai's formulation.

2. In addition, Desai does not teach another key claim limitation. Claim 1 requires that the analgesics of elements A and B differ in more than release rates. The claim also requires that the corresponding active analgesics in element A or element B must be either a *locally* acting or a *systemically* acting analgesic.

Desai's formulations provide the identical *systemically* acting analgesic, i.e., naproxen anion. It remains to be explained by Desai or other references of record how any single analgesic agent can be *both* a locally *and* a systemically acting analgesic. It is highly improbable that the naproxen anion can function locally and systemically. Desai does not teach or suggest that this is the case. Thus, it is far more likely that persons of ordinary skill in the art would not have understood Desai's formulation as providing both a local and a systemic acting analgesic.

Because Desai's formulation does not disclose or enable the claimed composition the rejection over Desai should be withdrawn.

3. In addition to the foregoing remarks, it is respectfully brought to Examiner's attention that the amended claims specify that the delayed and rapid release components provide distinct *active analgesic* compounds rather that distinct *chemical* compounds. In view of the established fact that Naproxen/Naproxen sodium provide the same active analgesic compound, the rejection should be withdrawn.

4. Last, it is brought to Examiner's attention that it is long-established Patent Office policy to grant and issue pharmaceutical patents possessing claims directed toward a "pharmaceutical compound and a salt thereof", in the same claim. From this, it can only be concluded that a pharmaceutical compound, e.g., naproxen, is not considered to be a functionally and patentably distinct compound from its salt, i.e., naproxen sodium.

If PTO policy were to view a pharmaceutical compound and its salt as distinct compounds, not only would they not be recited within the same claim, but they would be restricted out of the application. Thus, the general policy is to not distinguish between a pharmaceutical compound and a salt thereof as distinct functional entities. Clearly Examiner's rationale for maintaining the instant rejection runs counter to this longstanding policy and practice.

It is respectfully suggested that the newly amended claims submitted herewith are distinguishable from Desai. The claims require that elements A and B must have distinct active analgesic compounds. Desai teaches a compound and a salt that provide the identical active analgesic agent.

It is believed that in view of the foregoing remarks and amendments, that the claims are in condition for allowance.

It is respectfully requested that allowance be granted.

## CONDITIONAL PETITION FOR EXTENSION OF TIME

If any extension of time for this response is required, Applicants request that this be considered a petition therefore. Please charge the required fee to Deposit Account No. 14-1263.

## ADDITIONAL FEES

Please charge any further insufficiency of fees, or credit any excess to Deposit Account No. 14-1263.

Respectfully Submitted,

Norris, McLaughlin & Marcus
875 Third Avenue
New York, NY 10022
Telephone (212) 808-0700
Facsimile (212) 808-0844

Theodore Gottlieb, PhD
Reg. No. 42, 597

Certificate of Transmission

I hereby certify that this correspondence is being transmitted to the U.S. Patent and Trademark Office by deposit in the US POSTAL SERVICE as first class mail on Oct 1, 2004

AGATA GLINSKA
Typed or printed name of person signing this certificate

Signature Agata Glinska